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FINAL REPORT

RETINAL HEMORRHAGE AT HIGH ALTITUDE

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Of 20 men and women exposed to 5360 m. altitude hypoxia for periods of two to four weeks, all showed increased vascular tortuosity and dilatation and 13 showed retinal hemorrhages which were not found to cause scotomata by grid testing. Hemorrhages were asymptomatic and only weakly related to exertion, length of stay, or severity of other symptoms. These findings confirm our previous observations.

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SUMMARY

Numerous recent reports attest to the high incidence of retinal hemorrhage during sojurns at high altitude, but little is known of its pathogenesis, course, or long-term outcome. This study of 20 individuals exposed to 5360 m. altitude for two to six weeks was planned to (1) expand knowledge of the characteristics and pathogenesis of high altitude retinopathy (HAR, (2) define the course of retinal hemorrhage (HARH) over weeks and months, and (3)develop guidelines for prevention and management. The subjects were examined at sea level and then daily at altitude; they were photographed after mydriasis and studied with fluorescein angiography before and after Stage I and III exercise. Retinal hemorrhage was seen in 60% of subjects but was only weakly associated with exercise and not at all with Val Salva maneuver. We propose the term High Altitude Retinopathy (HAR) to describe the vascular dilatation and increased tortuosity, disc hyperemeia, and frequent retinal hemorrhage seen at high altitude. Visual scotomata matched retinal pathology in only one instance when one of several "cotton wool" spots fitted a demonstrated scotoma. No hemorrhages matched scotomata found by field studies and believed to be angio-scotomata, unrelated to altitude. We conclude that HAR is very common and that HARH affect over 60% of persons going to 5360 m. We found no evidence of long term effects though the studies will continue to follow some subjects for many months. Since thousands of mountain climbers and others are exposed, and have for years been exposed to even higher altitudes we do not consider HARH cause for immediate descent unless accompanied by other serious altitude illness.

INTRODUCTION: Since 1968 the Arctic Institute of North America has been conducting various studies of normal individuals exposed to high altitude. Scientists from five universities in Canada and the US participate in the research conducted annually on 12-16 volunteer subjects and on the scientists themselves. Support is provided by the National Institutes of Health and by the Department of Defence (Canada); in earlier years private sources also contributed. Support for this portion of the 1977 program was provided by the US Army.

The High Altitude Physiology Study (HAPS) is based at the Arctic Institute facility at 790 m. elevation on Kluane Lake in the Yukon Territory. There are two mountain establishments - Trench Camp at 3280 m. and Logan High at 5360 m. The latter is the site for most of the studies and includes several wood and/or fabric buildings on the summit plateau of Mt. Logan. These are heated, provided with electricity, and have comfortable working and living space. They are serviced by two STOL aircraft owned by the Arctic Institute. HAPS is conducted each year from early May to August and the facility is partially dismantled and stored during the winter.

Baseline and follow-up studies are conducted at McMaster Medical Center (Hamilton Ontario) and at the University of British Columbia in Vancouver. A variety of protocols are completed each year. A list of publications is appended.

OBJECTIVES: The purpose of this portion of the 1977 HAPS program was to examine retinal changes previously observed at altitude in order to: (1) better understand their patho-physiology, (2) establish whether or not persistent visual defects may result from altitude retinopathy, and (3) to support possible preventive or management strategies.

SPECIFIC BACKGROUND: In the course of the 1968 HAPS program, Houston noticed two persons with asymptomatic retinal hemorrhages which were not readily explained. Singh in 1969 reported retinal vein engorgement in 17 of 1925 Indian troops incapacitated by altitude illness during the Sino-Indian war of 1962. He observed papilledema and "vitreous hemorrhages" in 3 of these troops. Since 1968 the HAPS group has examined the retinae of most persons participating each year and Frayser has reported (1970, 1971) the incidence, characteristics, and possible etiology of retinal pathology in this group. Several others have subsequently reported similar observations among mountain climbers and from all reports the overall incidence of retinal hemorrhage at altitude appears to be 25-30%. Incidence appears to depend upon speed of ascent, altitude reached, and exertion, but other factors are probably

operative as well. Since it is easy to overlook some hemorrhages unless the pupils are dilated and photographs taken, it is likely that incidence is in reality much higher. With the exception of the rare pre-macular sub-hyaloid hemorrhages, most are asymptomatic and resolve spontaneously over a period of time not yet defined. Their basic mechanism is unknown. The only retinal abnormalities described until this report have been vascular engorgement and tortuosity, hyperemia, occasional papilledma, and hemorrhages. Two observers have reported persistent visual field defects in four mountaineers who had very severe altitude illness and retinopathy.

METHODS: The studies reported here follow the same general pattern of previous years but are more concentrated and specialized and will provide for the first time long term follow-up. The study population consisted of three groups: I Six climbers adapted to altitude by a ten day climb from 3280 to 5360 m. and a stay at that altitude of five weeks prior to being studied; II Seven climbers adapted by the ten day climb from 3280 to 5360 m. and examined immediately after arrival and daily thereafter; III Seven scientists flown to 5360 m. after a short stay at 3280 m. and examined daily for the week after arrival. When relevant, some data from the 1976 studies have been included. All baseline studies were done on Groups I and II at sea level but only some were completed on Group III.

Other study protocols performed on all groups were designed to examine responses to exertion, to hypoxemia during sleep, and to changes in pulmonary mechanics. These observations are not included here except where they bear directly on the purposes of this study; they are being reported elsewhere.

Based on the more sophisticated observations made in the course of this study we propose the term High Altitude Retinopathy (HAR) instead of the more restrictive term High Altitude Retinal Hemorrhage (HARH) which is a part of the over-all changes seen at altitude. Under HAR we include vascular engorgement and tortuosity, disc hyperemia, retinal hemorrhage, and "cotton wool" exudates.

Morphology of HAR: All 20 persons were examined by direct ophthalmoscopy each day at Logan High. Retinal photographs were taken at intervals as well as before and immediately after Stage I and III exercise on a bicycle ergometer. A Topcon TRC-F motorized camera with synchronized sequential flash and Kodachrome II film were used. Retinal vessel morphology, disc hyperemia, and number, character and location of hemorrhages were determined in the large number of photographs resulting. Retinal angiography was done

with one frame per second photography following intravenous injection of 5 ml of 10% fluorescein. Color photographs were taken before and after exercise on all 20 members of the three groups at Logan High. Fluorescein angiography was done on all 20 persons after exercise. Baseline angiography was done on the 13 persons in Groups I and II at sea level before the project start. Mydriasis was accomplished by instilling 10% neosynephrine and 0.5% tropicamide before all photography. Angiographic detail was confirmed and fluorescein leakage determined by examination of these photographs.

Examinations by direct ophthalmoscopy were done in a dark room, usually in the evening, without mydriasis. This portion of the study was largely descriptive and intended to identify the prevalence of various morphologic changes and their possible causal or temporal relationships to other activities or events.

Visual Acuity and Field Testing: The 13 members of Groups I and II were examined for 30° kinetic visual fields using a Buasch and Lombe Autoplot with a 0.5 mm white target. Lighting at sea level and altitude was not identical. Amsler grid subjective testing was also performed at sea level and at altitude. Visual acuity was measured with a standard Snellen chart at 6 m. and color vision was screened by Ishihara test plates.

Provocative Tests: In an effort to confirm or refute the possibility that certain normally performed activities might increase the liklihood of HAR, retinal photographs and fluorescein angiography were carried out on all 20 persons after Stage I and III exercise done in the course of another protocol. Because of the possibility that increased intra-thoracic pressure due to straining (such as normally occurs during lifting, soughing, or defecation), might, by increasing venous pressure, increase the occurrence of HAPH, open glottis Val Salva maneuvers were performed by all 20 persons at Logan High. This was done by having the individual maintain a pressure of 50 mm Hg (measured by sphygmomanometer) during a 15 second exhalataion. Retinae were inspected before and after two successive maneuvers, the sustained pressure being considered within the range normally reached in routine activities.

Correlation of HAR with Other Observations: As part of the entire project, data from arterial and venous blood samples, expired air, EEG and EKG tracings (the former while awake and also while asleep and monitored by oximeter as well), and daily clinical evaluations are being assembled but these data are not included in this report.

There appears to be no relationship between the symptoms of altitude illness and HAR or HARH, which confirms our impressions in previous years of this study.

RESULTS:

Morphology of HAR: All 20 persons in the three groups showed vascular dilatation and increased tortuosity at altitude as contrasted with sea level. This appeared in Groups II and III very shortly after arrival at altitude; we did not observe Group I until several weeks after arrival. Arterio-venous crossing changes were seen, perhaps because of the dilatation and tortuosity of both artery and vein within the relatively fixed diameter of the common scleral sheath at the crossing points. Many individuals showed hyperemia of the optic disc. Slight papilledema may be confirmed from inspection of stereo pairs on a few persons.

Retinal hemorrhages were noted in 13 of 20 persons studied in 1977, compared to appearance of RH in 7 of the 14 persons photographed in 1976, and to an approximate 30% incidence in persons examined (but not always photographed) in prior years. The overall incidence of 60% (in 1977) is higher than we and others have previously reported perhaps because of the ease with which RH are seen in the numerous photographs taken, compared to the difficulty of seeing all of the areas of the retina by direct inspection. We expect that when more photographs are taken more frequently on mountain climbing expeditions, the incidence of RH will be higher than now believed.

Most of the hemorrhages were flame-shaped and lay within the nerve fibre layer of the retina. A few hemorrhages were seen both in deeper or in more superficial layers. Many had pale centers. One subject showed numerous "cotton wool" spots in addition to hemorrhages. Members of all three groups were equally affected. RH appeared sporadically during the stay at altitude and were not limited to the period immediately after arrival or after tests. Many subjects showed loss of definition of the nasal margins of the optic disc as well as hyperemia of the disc, suggesting early papilledema; stereo pairs must be examined to confirm this.

Fluorescein angiography confirmed the above observations. In addition, 7 of the 20 persons examined in 1977 showed leakage of fluorescein in the area of the optic disc, a observation not previously reported. The subject with "cotton wool" spots showed leakage in the ischaemic areas as might be expected.

Visual Acuity and Visual Fields: No change in visual acuity was noted in all 13 members of Groups I and II. Five of the 13 persons tested with kinetic perimetry showed small absolute scotomata one of which coincided with one of the many "cotton wool" spots in the subject with these exudates. In no other subject did the location of a scotoma match any observed retinal abnormality or hemorrhage. Group III was not tested. Central vision was thought to be slightly abnormal in the subject with "cotton wool" spots but Amsler grid testing was normal in all others.

Provocative Testing: Photographs were taken before and immediately after measured exercise in 1977 as in 1976. Five of the total of 36 persons in the two years were found to have fresh hemorrhages developed during or immediately after exercise. None of the RH were symptomatic.

All 20 persons in the 1977 study were examined before and immediately after two successive Val Salva maneuvers; none were found to have developed fresh RH during the maneuver. Although photographs were not taken, we do not believe RH developing during or after this maneuver were overlooked.

DISCUSSION: High Altitude Retinopathy (HAR) which we define as vascular dilatation, increased vascular tortuosity and disc hyperemia with or without retinal hemorrhage (RH) appears to develop in most, and perhaps all individuals at the altitude we have been studying (5360 m.) There is insufficient evidence available to indicate at what altitude HAR begins to appear, though we believe it may be detected at considerably lower elevations. HAR may be considered a "normal" response to hypoxia and it is seen in persons hypoxic from pulmonary insufficiency at sea level as well as in well persons at altitude. This response becomes "abnormal" when vascular decompensation is apparent as evidenced by hemorrhages, "cotton wool" spots, and possible papilledema. Over the last seven years we have observed retinal hemorrhages in more than 35% of all persons at Logan High, but as techniques of vizualization and photography improve the percentage increases. HAR has been present in most all persons examined. Pale centers have been seen in a third of all hemorrhages photographed and may be manifestations of platelet micro-emboli or simply underlying normal retina seen through a thin portion of hemorrhage. Injected fluorescein can be seen behind the pale center in some instances indicating that this is not a light reflex. McCormick (personal communication) observed similar pale centers in hemorrhages seen in neo-nates especially after prolonged or forceps-assisted delivery. Though retinal hemorrhages are seen in about 25% of all neonates examined, their etiology is unknown. We have suggested that they may be due to hypoxia in utero or during delivery.

The finding of "cotton wool" spots in an otherwise healthy person at altitude suggests that significant retinal ischemia may occur at this altitude, the upper limit of where humans live permanently and close to the altitude at which deterioration outstrips adaptation to hypoxia. "Cotton wool" spots have not been previously reported and may have considerable patho-physiological implications.

Our studies show that RH may occur at any time after arrival at altitude and are not limited to the immediate adaptive period. Almost all are asymptomatic would not be known unless searched for carefully; even then some may be overlooked without photographic confirmation. There are suggestions that the onset of hemorrhage is rather abrupt and may be weakly associated with exertion, though not with a Val Salva maneuver. The precipitating cause of high altitude retinal hemorrhage is unknown; we believe the cause is multi-factorial.

Leakage of fluorescein around the disc margin was seen frequently in this series and seems most likely due to endothelial hypoxia and resulting increase in permeability at this vulnerable location. Similar leakage occurs in glaucoma, in ocular hypotony, and when spinal fluid pressure is elevated. The optic disc can be affected by any condition impairing oxygen delivery to this site.

The fact that there is only a weak relationship between exertion and RH and no association with the Val Salva maneuver suggessts that RH are due primarily to abnormality on the arteriolar side of capillaries. In previous years tonometry has not shown any change in intra-ocular pressure.

An important part of this study is the long-term follow-up of persons who have been found to have a major retinal abnormality at altitude. We shall be doing specialized field testing at the University of British Columbia with the help of Dr. Stephen Drance. This will be done by both kinetic and static methods, including static threshold cuts through the scotomata detected in 1977 at altitude. We will determine: (1) whether or not persistent visual field defects can be identified, and (2) whether additional parameters or methods should be added to our future studies.

This study adds further evidence that normal, healthy, asymptomatic individuals may have considerable retinopathy after climbing to 5380 m. and perhaps may develop this considerably below that altitude. Since scores of thousands of persons are exposed to this and higher altitudes during mountaineering or skiing or trekking expeditions, the subject is of considerable practical importance. Considering that hundreds of thousands of people have,

during the last hundred years, gone to altitudes where HAR and HARH can be expected without any reports of persistent eye pathology appearing in the medical literature, it seems unlikely that persistent or detectable visual defects may result. Finally, since many persons with acute or chronic hypoxia due to disease at sea level also show similar retinopathy, the subject has some clinical importance as well. We believe that altitude hypoxia is a valuable approach to the study of retinal pathology from other causes.

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